# Symproic® (naldemedine)

**Policy #** 00611
Original Effective Date: 04/18/2018
Current Effective Date: 04/18/2018

*Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.*

**When Services May Be Eligible for Coverage**
*Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:*

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Symproic®‡ (naldemedine) to be **eligible for coverage** when the patient selection criteria are met.

Patient Selection Criteria
Coverage eligibility for Symproic (naldemedine) will be considered when ALL of the following criteria are met:

- Patient has a diagnosis of opioid induced constipation (OIC); AND
- Patient has chronic, NON-cancer pain [including chronic pain related to PRIOR cancer or its treatment]; AND
- Patient is 18 years of age or older; AND
- Patient has been receiving opioids for at least 4 weeks or longer; AND
  *(Note: This specific patient criterion is an additional Company requirement, based on clinical trials, for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient does NOT have a known or suspected gastrointestinal obstruction; AND
- Patient has tried and failed standard therapy for the condition for an appropriate duration, including use of both fiber and laxative products, unless there is clinical evidence or patient history that suggests the use of fiber and laxative products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has tried and failed (e.g. intolerance or inadequate response) Amitiza®‡ (lubiprostone) AND Movantik®‡ (naloxegel) for an appropriate duration unless there is clinical evidence or patient history that suggests these agents will be ineffective or cause an adverse reaction to the patient.
  *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

**When Services Are Considered Not Medically Necessary**
Based on review of available data, the Company considers the use of Symproic (naldemedine) when the patient has NOT tried and failed the required pre-requisite therapies mentioned in the patient selection criteria to be **not medically necessary.****

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Based on review of available data, the Company considers the use of Symproic (naldemedine) when the patient has NOT been receiving opioids for at least 4 weeks or longer to be **not medically necessary.****

**When Services Are Considered Investigational**
*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Company considers the use of Symproic (naldemedine) when the patient selection criteria are not met (EXCEPT those denoted as **not medically necessary****) to be **investigational.***

## Background/Overview

Symproic is an opioid antagonist indicated for the treatment of opioid-induced constipation in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment. Symproic is available in 0.2 mg tablets and is dosed at 0.2 mg once daily with or without food.

**Opioid Induced Constipation**
According to guidelines from the American Academy of Pain Medicine (endorsed by the American Gastroenterological Association) recommend dietary (increased fluid, fiber) changes and over the counter options (stool softeners, laxatives, etc). If these do not provide adequate relief, drugs such as Movantik or Amitiza are options. Symproic would add to this list of options.

## FDA or Other Governmental Regulatory Approval

**U.S. Food and Drug Administration (FDA)**
Symproic is an opioid antagonist indicated for the treatment of opioid-induced constipation in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment.

## Rationale/Source

Symproic was evaluated in two replicate, 12-week, randomized, double-blind, placebo-controlled trials (Study 1 and Study 2) in which Symproic was used without laxatives in patients with OIC and chronic non-cancer pain. Patients receiving a stable opioid morphine equivalent daily dose of at least 30 mg for at least 4 weeks before enrollment and self-reported OIC were eligible for clinical trial participation. A total of 547 patients in Study 1 and 553 patients in Study 2 were randomized in a 1:1 ratio to receive Symproic 0.2 mg once daily or placebo for 12 weeks. The efficacy of Symproic was assessed in Studies 1 and 2 using a responder analysis. A responder was defined as a patient who had at least 3 spontaneous bowel movements per week and a change from baseline of at least 1 spontaneous bowel movement per week for at least 9 out of the 12 weeks and 3 out of the last 4 weeks in Studies 1 and 2.

In Studies 1 and 2, the mean increase in frequency of spontaneous bowel movements per week from baseline to the last 2 weeks of the 12-week treatment period was 3.1 for Symproic vs. 2.0 for placebo (difference 1.0, 95% CI 0.6, 1.5), and 3.3 for Symproic vs. 2.1 for placebo (difference 1.2, 95% CI 0.8, 1.7),

respectively. During week 1 of the treatment period, the mean increase in frequency of spontaneous bowel movements per week from baseline was 3.3 for Symproic vs. 1.3 for placebo (difference 2.0, 95% CI 1.5, 2.5) in Study 1 and 3.7 for Symproic vs. 1.6 for placebo (difference 2.1, 95% CI 1.5, 2.6) in Study 2. The mean increase in the frequency of complete spontaneous bowel movements per week from baseline to the last 2 weeks of 12-week treatment period was 2.3 for Symproic vs. 1.5 for placebo (difference 0.8, 95% CI 0.4, 1.2) in Study 1 and 2.6 for Symproic vs. 1.6 for placebo (difference 1.1, 95% CI 0.6, 1.5) in Study 2. A complete spontaneous bowel movement was defined as a spontaneous bowel movement that was associated with a sense of complete evacuation. The change in the frequency of complete spontaneous bowel movements without straining per week from baseline to the last 2 weeks of the treatment period was 1.3 for Symproic vs. 0.7 for placebo (difference 0.6, 95% CI 0.2, 0.9) in Study 1 and 1.8 for Symproic vs. 1.1 for placebo (difference 0.7, 95% CI 0.3, 1.2) in Study 2.

## References

1. Symproic [package insert]. Shinogi Inc. Florham Park, New Jersey. August 2017.

## Policy History

Original Effective Date: 04/182018
Current Effective Date: 04/18/2018
04/05/2018 Medical Policy Committee review
04/18/2018 Medical Policy Implementation Committee approval. New policy
Next Scheduled Review Date: 04/2019

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

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For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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**NOTICE:** Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.